mber of npared ABS	ABS	Study design	Year	Author	Title	Study population	Clinical outcome	Evidence level (adapted EBM Oxford)	Quality (NOS, RoB 2.0)	Delirium	Cognition	Mortality	Fall
1	ADS	RCT	2013	Kersten et al.	frail elderly population: a randomized controlled trial	Nursing home residents, n = 87 with a mean age of 85 years	Cognitive function Mouth dryness	1	Good	0	1	(,
2	CrAS, SCDL	Cohort study	2001	Han et al.	Use of Medications with Anticholinergic Effect Predicts Clinical Severity of Delirium Symptoms in Older Medical Inpatients	Inpatients with delirium, $n = 278$ with a mean age of 83.4 ± 7.3 years	Change in severity of delirium symptoms Dementia diagnosis	4	Poor	1	0	(,
1	CrAS	Cohort study	2008	Han et al.	Cumulative anticholinergic exposure is associated with poor memory and executive function in older men	Community-dwelling men, $n = 544$ with a mean age of 74.4 ± 5.2 years	Short term memory (HVRT) Executive function (IADL)	2a	Good	0	1	(,
1	ARS	Cohort study	2008	Rudolph et al.	The Anticholinergic Risk Scale and Anticholinergic Adverse Effects in Older Persons	Inpatient of 2 cohorts retrospective cohort: $n = 132$ with a mean age of 78.7 ± 5.3 years prospective cohort: $n = 117$ male with a mean age of 71.5 ± 11.6 years	Central and peripheral anticholinergic adverse effects (c: falls, dizziness, confusion, p: dry mouth, dry eye, constipation)	4	Poor	0	0	(
1	CrAS	Cohort study (reanalysis on a RCT)	2009	Agar et al.	Changes in anticholinergic load from regular prescribed medications in palliative care as death approaches	Palliative care patients, $n = 461$ with a mean age of 71 ± 12 years	Quality of life (McCill's Quality of life index) Functional outcome (Karnofsky performance scale)	4	Poor	0	0	(1
1	CrAS	Cohort study	2009	Juliebo et al.	Risk Factors for Preoperative and Postoperative Delirium in Elderly Patients with Hip Fracture	Orthopedic inpatients with hip fracture, $n = 364$ with a mean age of 84 ± 4 years	Delirium (CAM, pre- and postoperatively)	2a	Good	1	0	(1
1	ADS	Cohort study	2009	Low et al.	Use of medications with anticholinergic properties and cognitive function in a young-old community sample	Community-dwelling patients, $n = 2058$ with a mean age of 62.5 ± 1.5 years	Mild cognitive impairment	2a	Good	0	1	(,
1	ACB	Cohort study	2010	Campbell et al.	Use of anticholinergics and the risk of cognitive impairment in an African American population	Community-dwelling African American, $n=1652$ with a mean age of 81.8 ± 5.3 years	Cognitive Impairment	2a	Good	0	1	(,
1	CrAS	Cohort study	2010	Clark et al.	The impact of opioids, anticholinergic medications and disease progression on the prescription of laxatives in hospitalized palliative care patients: a retrospective analysis	Palliative care, $n = 211$ with a mean age of 72.3 ± 14.72 years	Prescription of laxatives	2b	Good	0	0	(
1	AAS	Cohort study	2010	Ehrt et al.	Use of drugs with anticholinergic effect and impact on cognition in Parkinson's disease: a cohort study	Community-based PD patients, $n = 235$ with a mean age of 74.7 \pm 8.4 years	Cognitive function (MMSE)	2a	Good	0	1	(1
1	Chew	Cohort study	2010	Jessen et al.	Anticholinergic drug use and risk for dementia: target for dementia prevention	Outpatients, n = 2605 and aged > 70 years	Dementia	4	Poor	0	0	(1
1	ACB	Cohort study	2011	Campbell et al.	Association between prescribing of anticholinergic medications and incident delirium: a cohort study	Hospitalized patients with cognitive impairment, $n = 147 \text{ aged} \ge 65 \text{ years}$	Delirium (CAM)	4	Poor	1	0	(1
1	ACB	Cohort study	2011	Fox et al.	The impact of anticholinergic burden in Alzheimer's Dementia-the Laser-AD study	Nursing & residual homes, in- and outpatients with Alzheimer dementia (AD), $n=224 \text{ with a mean age of } 81 \pm 7.4 \text{ years,}$	Cognitive function (MMSE, SIB, ADAS-COG score)	2a	Good	0	1	(
1	ACB	Cohort study (multicenter)	2011	Fox et al.	Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study	In- and outpatients with complete MMSE score and medication, $n = 12'250$ aged ≥ 65 years	Cognitive function (MMSE) Mortality	2a	Good	0	1	1	
1	ARS	Cohort study (multicenter)	2011	Kumpula et al.	Anticholinergic Drug Use and Mortality Among Residents of Long-Term Care Facilities: A Prospective Cohort Study	Hospital and long-term care, $n=1004$ ARS 0: $n=455$, with a mean age of 83.0 ± 10.0 years ARS 1-2: $n=363$, with a mean age of 80.5 ± 11.0 years ARS \geq 3: $n=186$, with a mean age of 78.7 ± 12.3 years	Mortality	2a	Good	0	0	. 1	
1	ARS	Cohort study (multicenter)	2011	Lowry et al.	Associations Between the Anticholinergic Risk Scale Score and Physical Function: Potential Implications for Adverse Outcomes in Older Hospitalized Patients	Inpatients, $n = 362$ with a mean age of 83.6 ± 6.6 years	Physical function (BI) Mortality LOS	2a	Good	0	0	1	
1	CrAS	Cohort study	2011	Sheehan et sl.	A Retrospective Analysis of Primary Diagnosis, Comorbidities, Anticholinergic Load, and Other Factors on Treatment for Noisy Respiratory Secretions at the End of Life	Inpatients dying in the palliative care unit, $n = 199$ with a mean age of 70.5 ± 14.8 years	Need for treatment of noisy respiratory excretions (NRS)	2b	Good	0	0	(
2	ADS, ARS	Cohort study	2012	Gouraud-Tanguy et al.	Analysis of iatrogenic risk related to anticholinergic effects using two scales in acute geriatric inpatient unit	Patients from the geriatric care unit, $n = 1379$ with a mean age of 85 ± 6 years	Total anticholinergic side effects Peripheral anticholinergic side effects Central anticholinergic side effects	4	Poor	0	0	(,
1	ARS	Cohort study	2012	Koshoedo et al.	Anticholinergic Drugs and Functional Outcomes in Older Patients Undergoing Orthopaedic Rehabilitation	Patients from a rehabilitation unit, $n = 117$ with a mean age of 79 ± 7 years, with ACH: $n = 38$ with a mean age of 77 ± 7 years and without ACH: $n = 79$ with a mean age of 80 ± 6 years	Functional outcome (BI) LOS	2a	Good	0	0	(·
1	ACB	Cohort study	2013	Koyama et al.	Ten-year trajectory of potentially inappropriate medications in very old women: importance of cognitive status	Community-dwelling women, n = 1484, at baseline with $n = 358$ users with a mean age of 78 ± 3.1 years and $n = 1115$ non-users with a mean age of 78 ± 3.2 years	Cognitive function (MCI) Dementia	4	Poor	0	1	(,

er of ared ABS	ABS	Study design	Year	Author	Title	Study population	Clinical outcome	Evidence level (adapted EBM Oxford)	Quality (NOS, RoB 2.0)	Delirium	Cognition	Mortali	ty :
3	ACB, ADS, ARS	Cohort study	2013	Mangoni et al.	LANTICHOUNGEROIC ACTIVITY AND AU-CAUSE POST DISCHARGE	Patients with hip fractures and planned surgery, $n = 71$ with a mean age of 84 ± 6 years	Postoperative complications LOS 3 month all-cause mortality 1 year all-cause mortality	2a	Good	0	0		1
1	CrAS	Cohort study	2013	Yeh et al.	Lanticholinergic burden for demented older adults: A	Veteran home demented residents, n = 53 with a mean age of 83.4 years	Cognitive function (MMSE) Functional outcome (BI)	4	Poor	0	1		0
1	ARS	Cohort study	2014	Dispennette et al.	Drug Burden Index score and anticholinergic risk scale as predictors of readmission to the hospital	Inpatients, n = 229 with a mean age of 78 years	Risk of hospital readmission	4	Poor	0	0		0
2	ADS, ARS	Cohort study	2014	Kalisch et al.	Multiple Anticholinergic Medication Use and Risk of Hospital Admission for Confusion or Dementia	Australian veterans, n = $36'015$ with a mean age of 82.9 ± 6.8 years	Risk of hospitalization for confusion or dementia	2b	Good	0	0	,	(
3	ACB, ADS, ARS	Cohort study	2014	Kashyap et al.	Laccociations Retween Anticholinergic Dring Use and Incident	Outpatient clinics without dementia or depression, $n = 102$ with a mean age of 71.9 ± 7.3 years	Cognitive function (MMSE, GDP)	4	Poor	0	1		(
1	ACB	Cohort study (multicenter)	2014	Kidd et al.	The relationship between total anticholinergic burden (ACB) and early in-patient hospital mortality and length of stay in the oldest old aged 90 years and over admitted with an acute illness	Inpatients, $n = 419$ with a median age of 92.9 years, ACB 0: $n = 163$ with a median age of 93.4 years ACB 1: $n = 142$ with a median age of 92.9 years ACB \geq 2: $n = 114$ with a median age of 92.5 years	Mortality LOS	2b	Good	0	0	1	1
1	ACB	Cohort study (multicenter)	2014	Koyama et al.	Long-term cognitive and functional effects of potentially inappropriate medications in older women	Community-dwelling women, $n = 1429$ with a mean age of 83.2 ± 3.3 years	Functional outcome (IADL) Cognitive function (MMSE)	4	Poor	0	1		
1	ARS	Cohort study (multicenter)	2014	Landi et al.	Anticholinergic Drug Use and Negative Outcomes Among the Frail Elderly Population Living in a Nursing Home	Nursing homes residents, n = 1490 with a median age of 83.56 years	Functional decline Falls Delirium	2a	Good	1	0		•
1	ARS	Cohort study	2014	Walter et al.	Perioperative Anticholinergic Medications and Risk of Catheterization After Urogynecologic Surgery	Female outpatients, n = 125, ACH 0-7: n = 98 with a mean age of 56.0 ± 12.1 years ACH ≥ 8 : n = 27 with a mean age of 55.3 ± 11.2 years	Failed post-operative void trial	2b	Good	0	0	1	
1	ARS	Cohort study	2014	Zimmerman et al.		Palliative inpatients, $n = 217$ with a mean age of 72.9 ± 12.8 years	Delirium (Chart review)	4	Poor	1	0		
1	ADS	Cohort study	2015	Block et al.	Leganitiva hiirdan on naiironevehological tiinetion in a gariatrie	Primary care patients (outpatients), n = 290 with a mean age of 72.76 ± 5.47 years	Neuropsychological functions (RBANS test)	4	Poor	0	1		
1	ARS	Cohort study	2015	De La Cruz et al.	1	Women undergoing urodynamics, $n = 599$, low ACH: $n = 440$ with mean age of 57.2 ± 14 years high ACH: $n = 159$ with mean age of 56.3 ± 12.9 years	Bladder function	4	Poor	0	0		
1	ADS	Cohort study	2015	Gupte et al.	Impact of anticholinergic load of medications on the length of stay of cancer patients in hospice care	Cancer patients discharge from hospice care, selected by ICD-9 codes 140 - 239, n = 1801 ADS 0-2: n = 641, mean age of 72.38 \pm 13.50 years ADS 3-5: n = 637, mean age of 71.75 \pm 13.83 years ADS \geq 6: n = 523, mean age of 70.42 \pm 13.79 years	LOS / survival in hospice care (US)	2b	Good	0	0		
1	ATS	Cohort study	2015	THerner et al		Psychiatric patients with TDM, n = 69 with a mean age of 74.3 ± 5.7 years	Anticholinergic side effects (peripheral and central)	4	Poor	0	0		
1	ARS	Cohort study	2015	Lu et al.	ē	Using the Taiwan's National Health Insurance Research Database (NHIRD), n = 59'042 aged > 65 years	All-cause admission to hospital Fracture-specific admission to hospital Death	2b	Good	0	0	,	
1	ACB	Cohort study	2015	1	Total anticholinergic burden and risk of mortality and cardiovascular disease over 10 years in 21,636 middle-aged and older men and women of EPIC-Norfolk prospective population study	Community-dwelling patients without cancer, $n=21'636$ ACB 0: $n=17'317$ with mean age of 57.9 ± 9.1 years ACB 1: $n=2704$ with mean age of 62.9 ± 8.8 years ACB 2-3: $n=1324$ with mean age of 62.2 ± 9.2 years ACB > 3 : $n=291$ with mean age of 63.1 ± 8.9 years	All-cause mortality Incident CVD	2b	Good	0	0		
1	ACB	Cohort study	2015	Richardson et al.	, ,	Community-dwelling patients without dementia, $n = 2696 \text{ aged} \ge 65 \text{ years},$ men (m) $n = 1286 \text{ and women (w) } n = 1410$	Injurious falls (m/f) Any falls (m/f) Total number of falls (m/f)	2a	Good	0	0		
8	ACB, ADS, ARS, ABC, ACL, Chew, CrAS, AAS	Cohort study	2015	Salahudeen et al.	l 1	Outpatients, $n = 537'387$ with a mean age of 74.7 ± 7.6 years	Hospital admissions Falls-related hospitalizations LOS GP visits	2b	Good	0	0	1	
2	ADS, ARS	Cohort study	2015	Wolters et al.	Anticholinergic Medication Use and Transition to Delirium in Critically Ill Patients: A Prospective Cohort Study	Critically ill inpatients, n = 1112 with a mean age of 60 ± 16 years	Delirium onset (ICU-CAM)	2a	Good	1	0	i	

r of	ABS	Study design	Veer	Author	Title	Study population	Clinical outcome	Evidence level	Quality	Delirium	Cognition	Mortal	itv
red ABS	ADS	Study design	1 cai	Author		Community-dwelling and outpatients with Parkinson,	Cinical outcome	(adapted EBM Oxford)	(NOS, RoB 2.0)	Demium	Cognition	Violtan	
1	ADS	Cohort study	2015	Yarnall et al.	Anticholinergic Load: Is there a Cognitive Cost in Early Parkinson's Disease?	PD-ADS 0: $n = 112$ with a mean age of 68.6 ± 8.9 years PD+ADS ≥ 1 : $n = 84$ with a mean age of 69.7 ± 7.7	Mild cognitive impairment in Parkinson's disease	4	Poor	0	1		0
1	ACB	Cohort study	2016	Campbell et al.	Association of Anticholinergic Burden with Cognitive Impairment and Health Care Utilization Among a Diverse Ambulatory Older Adult Population	Community-dwelling patients, $n = 3344 \text{ aged} \ge 65 \text{ years}$	Cognitive impairment Inpatient, ED and outpatient visit	2b	Good	0	1		0
1	ARS	Cohort study	2016	Crispo et al.	Associations between Anticholinergic Burden and Adverse Health Outcomes in Parkinson Disease	Patients with Parkinson disease, n = 16'302 aged ≥ 40 years	Delirium Fracture 30-day hospital revisits	2b	Good	1	()	0
1	ADS	Cohort study (reanalysis on a RCT)	2016	Hochman et al.	Anticholinergic Drug Burden in Noncancer Versus Cancer Patients Near the End of Life	Comparing patients with cancer $n=126$ with a mean age of 79.1 ± 10.6 years and without cancer $n=118$ with a mean age of 69.7 ± 10.5 years	Fatigue Quality of life (QOL) (worse) Drowsiness Well-being	4	Poor	0	()	0
1	ARS	Cohort study	2016	Mangoni et al.	Heat Waves, Drugs with Anticholinergic Effects, and Outcomes in Older Hospitalized Adults	Hospitalized patients $n = 307$ in heat waves period with a median age 78 years, $n = 1114$ during non heat waves period with a median age 77 years	LOS In-hospital mortality	2b	Good	0	()	1
1	ACB	Cohort study	2016	Vetrano et al.	Anticholinergic Medication Burden and 5-Year Risk of Hospitalization and Death in Nursing Home Elderly Residents With Coronary Artery Disease	Nursing home residents, $n = 3781$ with a mean age of 83 ± 7 years	Hospitalization Mortality	2b	Good	0	()	1
1	DS	Cohort study (multicenter)	2017	Burry et al.	Delirium and exposure to psychoactive medications in critically ill adults: A multi-centre observational study	Critically ill adults admitted to the ICU, $n = 520 \text{ aged} \ge 18 \text{ years}$	Delirium (ICDSC)	2a	Good	1	()	
3	ACB, ADS, ARS	Cohort study	2017	Cossette et al.	Association Between Anticholinergic Drug Use and Health- Related Quality of Life in Community-Dwelling Older Adults	Community-dwelling patients free of disabilities in ADL and cognitive impairment, $n=1793$ with a mean age of 74.4 ± 4.2 years	Mental Component Summary (MCS) Physical Component Summary (PCS)	4	Poor	0	1		
1	ACB	Cohort study (multicenter)	2017	Cross et al.	Potentially Inappropriate Medication, Anticholinergic Burden, and Mortality in People Attending Memory Clinics	Community-dwelling patients with mild cognitive impairment or dementia of 9 memory clinics, $n = 964$ with a mean age of 77.6 ± 7.4 years	Mortality	2a	Good	0	()	
3	ACB, ARS, Chew	Cohort study	2017	Egberts et al.	Anticholinergic drug exposure is associated with delirium and post discharge institutionalization in acutely ill hospitalized older patients	Acutely ill, hospitalized patients (> 3 days), $n = 905$ with a mean age of 81.0 ± 7.03 years	Delirium on admission LOS Post discharge institutionalization In hospital mortality	2b	Good	1	()	
2	ARS, DS	Cohort study (multicenter)	2017	Gutierrez et al.	Anticholinergic burden and health outcomes among older adults discharged from hospital: results from the CRIME study	Inpatients total, $n=921$ with mean age of 81.2 ± 7.4 years For ARS: ARS 0: $n=740$ with a mean age of 80.9 ± 7.3 years ARS 1: $n=132$ with a mean age of 82.6 ± 72 years ARS ≥ 2 : $n=49$ with a mean age of 81.1 ± 7.8 years For Duran: Duran 0: $n=625$ with a mean age of 80.7 ± 7.3 years Duran 1: $n=218$ with a mean age of 82.0 ± 7.4 years Duran ≥ 2 : $n=78$ with a mean age of 82.1 ± 7.1 years	Mortality within 1 year of discharge Rehospitalization within 1 year of discharge	4	Poor	0	()	
1	ADS	Cohort study (multicenter)	2017	Jean-Bart et al.	Exposure to anticholinergic and sedative medicines as indicators of high-risk prescriptions in the elderly	Inpatients, $n = 315$ with a mean age of 86.6 ± 6.2 years	Risk of falls	2a	Good	0	()	
1	ACB	Cohort study	2017	Naharci et al.	Effect of anticholinergic burden on the development of dementia in older adults with subjective cognitive decline	Patients with subjective cognitive decline, $n = 109$ with a mean age 72.5 ± 63 years	Dementia	2b	Good	0	()	
1		Cohort study	2017	Sarbacker et al.	elderly Mexican Americans	Mexican Americans, n = 1497 with a mean age of 74.56 years	Mortality	2b	Good	0	(,	
1		Cohort study (for part of outcomes)	2017	Sevilla-Sanchez et al.	Adverse drug events in patients with advanced chronic conditions who have a prognosis of limited life expectancy at hospital admission	Inpatients requiring palliative care, $n = 235$ with a mean age of 86.8 ± 5.37 years	Survival	2a	Good	0	()	
1	ADS	Cohort study	2017	Weglinski et al.	Prospective evaluation of mouth and eye dryness induced by antimuscarinic drugs used for neurogenic overactive bladder in 35 patients with multiple sclerosis	Community-dwelling patients with MS, $n = 35$ with a mean age of 50.1 ± 10.2 years	Eye dryness (Xerophtalmia) Mouth dryness (Xerostomia)	4	Poor	0	()	
2	ACB, ARS	Cohort study	2017	Wen-Han Hsu et al.	Comparative Associations Between Measures of Anti- cholinergic Burden and Adverse Clinical Outcomes	Inpatients, n = 116'043 aged > 65 years	Emergency Department Visits All-Cause Hospitalizations Fracture-Specific Hospitalization Incident dementia	2b	Good	0	()	
1	ATS	Cohort study	2017	Xu et al.	Assessing and predicting drug-induced anticholinergic risks: an integrated computational approach	Patients, exposed $n = 287'614$ and unexposed $n = 287'614$, with a mean age of 37.97 ± 18.79 years	Anticholinergic ADE	2b	Good	0	()	

•	olinergic burden scale ntified validation stud		on cli	ınıcal outcomes - a	systematic review, EJCP, Lisibach A et al, Corresponding	author: Pr Chantal Csajka ,Center for Research and I	nnovation in Clinical Pharmaceutical Sciences, Rue	du Bugnon 17, 1005	Lausanne		
Number of compared ABS			Year	Author	Title	Study population	Clinical outcome	Evidence level (adapted EBM Oxford)	Quality (NOS, RoB 2.0)	Delirium Cognition	n Mortality Falls
2	ACB, ARS	Cohort study	2018	Brombo et al.	Association of Anticholinergic Drug Burden with Cognitive and Functional Decline Over Time in Older Inpatients: Results from the CRIME Project	Inpatients n = 1123 with a mean age of 81 ± 7.5 years	Cognitive status (MMSE) Functional status (ADL)	4	Poor	0	0
1	ACB	Cohort study	2018	Campbell et al.	Anticholinergics Influence Transition from Normal Cognition to Mild Cognitive Impairment in Older Adults in Primary Care	Community-dwelling people, $n = 350$ with a mean age of 71.2 ± 5.1 years	Transition from normal to MCI in patients w/o dementia	2a	Good	0	0
1	ARS	Cohort study	2018	Clarke et al.	Association Between Objectively Measured Physical Activity and Opioid, Hypnotic, or Anticholinergic Medication Use in Older People: Data from the Physical Activity Cohort Scotland Study	Older people from the Physical Activity Cohort Scotland - Community-dwelling, $n=310$ with a mean age 77.3 ± 7 years	Physical activity	4	Poor	0	0
1	ACB	Cohort study	2018	Gamble et al.	Baseline anticholinergic burden from medications predicts incident fatal and non-fatal stroke in the EPIC-Norfolk general population	Outpatients, $n = 21'722$ with a mean age of 58.9 ± 9.2 years	Incident stroke Stroke mortality	2b	Good	0	
3	ACB, ADS, ARS	Cohort study (in an intervention study)	2018	Jaïdi et al.	Threshold for a Reduction in Anticholinergic Burden to Decrease Behavioral and Psychological Symptoms of Dementia	Inpatients with dementia and hospitalized for behavioral and psychological symptoms (BPSD), $n=147$ with mean age of 84.1 ± 5.2 years	Clinical and statistical significant improvement in BPSD when ACH load is reduced	2a	Good	0	0
1	ARS	Cohort study	2018	Kose et al.	Assessment of aspiration pneumonia using the Anticholinergic Risk Scale	Patients from a rehabilitation ward, n = 618 with a median age of 79 years with ACH: n = 162 with a median age of 80 years and without ACH: n = 456 with a median age of 78 years	Aspiration pneumonia	2b	Good	0	0
1	ARS	Cohort study	2018	Kose et al.	Anticholinergic load negatively correlates with recovery of cognitive activities of daily living for geriatric patients after stroke in the convalescent stage	Geriatric patients from a rehabilitation center, n = 418 patients with median age of 78 years	Functional recovery after stroke	2b	Good	0	0
1	ACB	Cohort study (multicenter)	2018	Lattanzio et al.	Anticholinergic burden and 1-year mortality among older patients discharged from acute care hospital	Patients discharged from acute care hospitals, $n = 807$ with a mean age of 81.0 ± 7.4 years	Mortality	2a	Good	0	1
1	ADS	Cohort study (for part of outcomes)	2018	Sevilla-Sanchez et al.	Prevalence, risk factors and adverse outcomes of anticholinergic burden in patients with advanced chronic conditions at hospital admission	Inpatients requiring palliative care, $n = 235$ with a mean age of 86.8 ± 5.37 years	Days of hospital stay Destination after discharge Inhospital mortality 1-year survival	2a	Good	0) 1
1	ACB	Cohort study	2018	Tan et al.	Anticholinergic burden and risk of stroke and death in people with different types of dementia	Patients with different dementia subtypes, $n = 39'107$ with a mean age of 79.9 ± 7.9 years	Stroke All-cause mortality	2b	Good	0	1
1	ADS	Cohort study	2018	Tiisanoja et al.	Anticholinergic burden and dry mouth among Finnish, community-dwelling older adults	Community-dwelling, non-smoking, dentate patients, $n=152$ with a mean age of 79.4 ± 3.67 years	Xerostomia Low unstimulated salivary secretion	4	Poor	0	0
1	ACB	Cohort study	2018	Ziad et al.	Anticholinergic drug use and cognitive performances in middle age: findings from the CONSTANCES cohort	Participants living in France, n = 34'267 aged 45-70 years	Cognitive performance (episodic memory, verbal fluency, executive functions)	2b	Good	0	0
1	ACB	Cohort study	2019	Ah et al.	Effect of anticholinergic burden on treatment modification, delirium and mortality in newly diagnosed dementia patients starting a cholinesterase inhibitor: A population-based study	Patients with cholinesterase inhibitor treatment for dementia, $n = 7438$ aged > 60 years ACB > 3 : $n = 1554$ ACB ≤ 1 : $n = 5884$	Delirium (ICD-10 F5.0) Mortality	2b	Good	1	
4	ACB, ADS, ARS, DS	Cohort study (reanalysis on a RCT)	2019	Andre et al.	Anticholinergic exposure and cognitive decline in older adults: effect of anticholinergic exposure definitions in a 3-year analysis of the multidomain Alzheimer preventive trial (MAPT) study	Community-dwelling French adults, $n=1396$ with a mean age of 75.2 ± 4.4 years	Cognitive decline (assessed with a composite score following MMSE, Free and Cued Selective Reminding Test, Category Naming Test, Digit Symbol Substitution Test)	2a	Good	0	1 0
1	ACB	Cohort study (multicenter)	2019	Corsonello et al.	The excess mortality risk associated with anticholinergic burden among older patients discharged from acute care hospital with depressive symptoms	Hospitalized patients in 7 acute care centers, $n = 576$ with a mean age of 79.6 ± 7.0 years	Mortality at 1-year after discharge	2a	Good	0	1
1	ACB	Cohort study	2019	Green et al.	Drugs Contributing to Anticholinergic Burden and Risk of Fall or Fall-Related Injury among Older Adults with Mild Cognitive Impairment, Dementia and Multiple Chronic Conditions: A Retrospective Cohort Study	Patients with impaired cognition, $n = 10'698$ with a mean age of 79.1 ± 7.99 years	Falls Falls related injuries	2b	Good	0	0
1	АСВ	Cohort study (in a RCT)	2019	Joshi et al.	Verbal learning deficits associated with increased anticholinergic burden are attenuated with targeted cognitive training in treatment refractory schizophrenia patients	Schizophrenic patients, intervention group $n=24$ with a mean age of 34.54 ± 12.13 years and control group $n=22$ with a mean age of 35.73 ± 13.0 years	Learning verbal training in intervention group Learning verbal training in control group	4	Poor	0	0
1	ACB	Cohort study	2019	Szabo et al.	Association between cumulative anticholinergic burden and falls and fractures in patients with overactive bladder: US-based retrospective cohort study	Outpatients with overactive bladder, n = 154'432 with a mean age of 55.7 years	Falls Fractures	2b	Good	0	0

mber of npared ABS	ABS	Study design	Year	Author	Title	Study population	Clinical outcome	Evidence level (adapted EBM Oxford)	Quality (NOS, RoB 2.0)	Delirium	Cognition	Mortality	Fal
1	I ADS	Nested Case- Control study	2016	Chatterjee et al.	Anticholinergic Medication Use and Risk of Dementia Among Elderly Nursing Home Residents with Depression	Uses 2007 to 2010 Minimum Data Set linked Medicare data set from all states (US), n =191'304 with depression and no baseline dementia, incidence matched cohort n = 141'940 with n = 28'388 cases and n = 113'552 controls, mean age of 80 years	Dementia	3	Good	0	0	C	
2	MACR ADS	Nested Case- Control study	2016	Chatterjee et al.	Anticholinergic Medication Use and Risk of Fracture in Elderly Adults with Depression	Uses 2007 to 2010 Minimum Data Set linked Medicare data set from all states (US), $n = 352'937$ with depression and no baseline fractures or falls in 2007, incidence matched cohort $n = 202'260$ with $n = 161'808$ controls and $n = 40'452$ cases, mean age of 81.4 ± 7.4 years	Fracture risk	3	Good	0	0	C	
1	I ACB	Case-Control study	2016	Zia et al.	Anticholinergic burden is associated with recurrent and injurious falls in older individuals	Patients, $n = 263$ cases with a mean age of 75.3 ± 7.3 years and $n = 165$ controls with a mean age of 72.13 ± 5.5 years	Recurrent and injurious falls	3	Good	0	0	C	1
1	I ADS	Nested Case- Control study	2017	Chatterjee et al.	Risk of Mortality Associated with Anticholinergic Use in Elderly Nursing Home Residents with Depression	Uses 2007 to 2010 Minimum Data Set linked Medicare data set from all states (US), n = 433'812 with depression, incidence matched cohort n = 224'740 with n= 179'792 controls and n = 44'948 cases, mean age of 83 years	Risk of mortality	3	Good	0	0	1	
1	HADS	Nested Case- Control study	2017	Lampela et al.	Anticholinergic Exposure and Risk of Pneumonia in Persons with Alzheimer's Disease: A Nested Case-Control Study	Community-dwelling patients diagnosed with AD, cases $n = 12'442$ with a mean age of 83.3 ± 6.7 years, controls $n = 24'349$ with a mean age of 83.3 ± 6.5 years	Risk of pneumonia	3	Good	0	O	C	
1	ADS	Case-Control study (multicenter)	2018	Aldebert et al.	Association of Anticholinergic Drug Use With Risk for Late Age-Related Macular Degeneration	Patients from 4 French ophthalmologic centers, n = 400 with cases $n = 200$ with a mean age of 74.8 ± 9.2 years and controls $n = 200$ with a mean age of 75.5 ± 7.2 years	Late Age-Related Macular Degeneration	4	Poor	0	0	C	1
1	I ARS	Nested Case- Control study	2018	Kose et al.	Anticholinergic drugs use and risk of hip fracture in geriatric patients	Patients from a rehabilitation ward, n = 601 with a median age of 79 years, fracture group n = 68 with a median age of 80.5 years and non-fracture group n = 533 with a median age of 79 years	Hip fracture	3	Fair	0	0	C	1
1	ARS	Case-Control study	2018	Machado-Duque et al.	Drugs With Anticholinergic Potential and Risk of Falls With Hip Fracture in the Elderly Patients: A Case-Control Study	Outpatients, cases $n = 300$ and controls $n = 600$ with a mean age of 81.6 years	Falls with hip fracture	3	Good	0	0	C	1
1	I ACB	Nested Case- Control study	2018	Richardson et al.	Anticholinergic drugs and risk of dementia: case-control study	Outpatients, aged \geq 65 years n = 40'770 cases and n = 283'933 controls (matching 1:7)	Incidence of dementia	4	Poor	0	0	C	1
1	CI, PI	Cross-sectional	2004	Minzenberg et al.	Association of anticholinergic load with impairment of complex attention and memory in schizophrenia	Outpatients with schizophrenia or schizoaffective disorders $n=106$ with a mean age of 39.9 ± 11.3 years	Simple attention Complex attention Short-term memory	5	Poor	0	1	C	r
1	I ACB	Cross-sectional	2009	Kolanowski et al.	A Preliminary Study of Anticholinergic Burden and Relationship to a Quality of Life Indicator, Engagement in Activities, in Nursing Home Residents With Dementia	Nursing home residents with dementia, $n = 87$ with a mean age of 85.7 ± 6.3 years	Quality of life: Multiple engagement observations	5	Good	0	0	C	1
1	ARS	Cross-sectional	2011	Lowry et al.	Clinical and demographic factors associated with antimuscarinic medication use in older hospitalized patients	Inpatients, $n = 362$ with a mean age of 83.6 ± 6.6 years	Institutionalization and comorbidities	5	Poor	0	0	C	r
1	I ARS	Cross-sectional	2011	Teramura- Gronblad et al.	Use of Anticholinergic Drugs and Cholinesterase Inhibitors and Their Association with Psychological Well-Being Among Frail Older Adults in Residential Care Facilities	Nursing homes, $n = 1475$ with a mean age of 81.7 ± 7.6 years	Psychological well-being	5	Poor	0	0	C	!
1	I ADS	Cross-sectional	2012	Drag et al.	Prescribing Practices of Anticholinergic Medications and Their Association With Cognition in an Extended Care Setting	Inpatients non-demented and non-delirious, $n=450$ with a mean age of 67.9 ± 10.5 years	Cognitive function	5	Poor	0	1	C	1
1	I ARS	Cross-sectional	2013	Bostock et al.	Associations between different measures of anticholinergic drug exposure and Barthel Index in older hospitalized patients	Consecutive series of community-dwelling and institutionalized settings, acute geriatric admission, $n = 271$ with a mean age of 83 ± 7 years	Barthel Index (physical function) AMT (Abbreviated Mental Test)	5	Good	0	1	C	
1	ADS	Cross-sectional	2013	Kersten et al.	Higher anticholinergic drug scale (ADS) scores are associated with peripheral but not cognitive markers of cholinergic blockade. Cross sectional data from 21 Norwegian nursing homes	Nursing home residents, n = 87 with a mean age of 73 years	Cognitive function (MMSE) Functional outcome (ADL)	5	Poor	0	1	С	
3	ADS, ARS, Chew	Cross-sectional	2013	Lampela et al.	Anticholinergic Drug Use, Serum Anticholinergic Activity, and Adverse Drug Events Among Older People: A Population Based Study	Community-dwelling, $n = 621$ with a mean age of 81.7 ± 4.9 years	Adverse events Cognitive function (MMSE, GDP) Functional outcome (ADL, IADL)	5	Poor	0	1	С	

-			t on cli	nical outcomes - a	systematic review, EJCP, Lisibach A et al, Corresponding	author: Pr Chantal Csajka ,Center for Research and I	nnovation in Clinical Pharmaceutical Sciences, Rue	du Bugnon 17, 1005 I	ausanne		_
Appendix 6b: Ide	ntified validation stud	ies (total n=104).							1		
Number of compared ABS	ABS	Study design	Year	Author	Title	Study population	Clinical outcome	Evidence level (adapted EBM Oxford)	Quality (NOS, RoB 2.0)	Delirium Cognition	Mortality Falls
2	2 ACB, ARS	Cross-sectional	2013	Pasina et al.	Association of anticholinergic burden with cognitive and functional status in a cohort of hospitalized elderly: comparison of the anticholinergic cognitive burden scale and anticholinergic risk scale: results from the REPOSI study	Hospitalized patients, $n = 1232$ with age of ≥ 65 years	Cognitive function (SBT) Physical function (BI)	5	Poor	0 1	0 0
1	ACB	Cross-sectional	2014	Lanctot et al.	Assessing Cognitive Effects of Anticholinergic Medications in Patients With Coronary Artery Disease	Outpatients with coronary artery disease, $n = 131$ with a mean age of 64.2 ± 9.1 years	Attention, speed, executive function	5	Poor	0 0	0 0
1	ADS	Cross-sectional	2015	Moulis et al.	Exposure to Atropinic Drugs and Frailty Status	Patients attending a geriatric frailty clinic, $n = 437$ with a mean age of 83.05 ± 6.15 years	Frailty	5	Poor	0 0	0 0
1	ACB	Cross-sectional	2016	O'Dwyer et al.	Association of anticholinergic burden with adverse effects in older people with intellectual disabilities: an observational cross-sectional study	Patients with intellectual disability, $n = 736 \text{ aged} \ge 40 \text{ years}$	Daytime dozing Constipation	5	Poor	0 0	0 0
2	ACB, ADS	Cross-sectional	2017	Ang et al.	The Impact of Medication Anticholinergic Burden on Cognitive Performance in People With Schizophrenia	Outpatients and inpatients with schizophrenia, $n = 705$ with a mean age of 39.18 ± 9.71 years	Cognitive performance (executive functions, fluency/memory, speed/vigilance)	5	Poor	0 1	0 0
5	ACB, ADS, ARS, Chew, CrAS	Cross-sectional	2017	Dauphinot et al.	Anticholinergic drugs and functional, cognitive impairment and behavioral disturbances in patients from a memory clinic with subjective cognitive decline or neurocognitive disorders	Older outpatients visiting memory clinic, $n = 473$ with a mean age of 80.58 ± 7.48 years	Functional impairment (Functional and global cognitive performances, as well as the behavioral and psychological symptoms of dementia)	5	Poor	0 1	0 0
1	ADS	Cross-sectional	2017	Eum et al.	Cognitive burden of anticholinergic medications in psychotic disorders	Patients with schizophrenia, schizoaffective and bipolar disorders, n = 483 with a mean age 36 years	Cognitive function (BACS) if ADS ≥4	5	Poor	0 1	0 0
8	ACB, ADS, ARS, ABC, ACL, Chew, CrAS, CABS	Cross-sectional	2017	Mayer et al.	Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives	Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years	Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives	5	Poor	0 1	0 1
1	ACB	Cross-sectional	2017	Pfistmeister et al.	Anticholinergic burden and cognitive function in a large German cohort of hospitalized geriatric patients	Hospitalized patients, $n = 89'579$ with a median age of 82 years, complete case analysis for cognitive impairment $n = 59'007$ and for dementia $n = 68'388$	Cognitive Impairment (MMSE) Dementia	5	Poor	0 1	0 0
1	ACB	Cross-sectional	2017	L'equitequilae at al	Anticholinergic Burden and Cognition in Older Patients With Schizophrenia	Community-dwelling patients with schizophrenia or schizoaffective disorder, $n = 60$ with a mean age of 63.6 ± 6.83 years	Alzheimer's dementia-related cognitive functions	5	Poor	0 1	0 0
1	АСВ	Cross-sectional	2018	Ablett et al.	A high anticholinergic burden is associated with a history of falls in the previous year in middle-aged women: findings from the Aberdeen Prospective Osteoporosis Screening Study	Community-dwelling women, $n = 3883$ with a mean age of 54.33 ± 2.27 years	History of falls	5	Poor	0 0	0 1
1	ACB	Cross-sectional	2019	Pasina et al.	Relation Between Delirium and Anticholinergic Drug Burden in a Cohort of Hospitalized Older Patients: An Observational Study	Inpatients, $n=502$, with delirium $n=151$ with a mean age of 85.0 ± 6.5 years, without delirium $n=32$ with a mean age of 83.4 ± 6.5 years	Delirium (4 AT)	5	Poor	1 0	0 0